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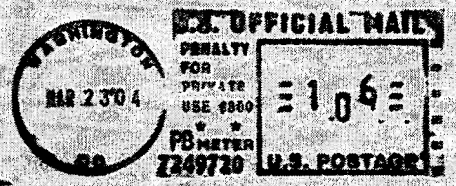

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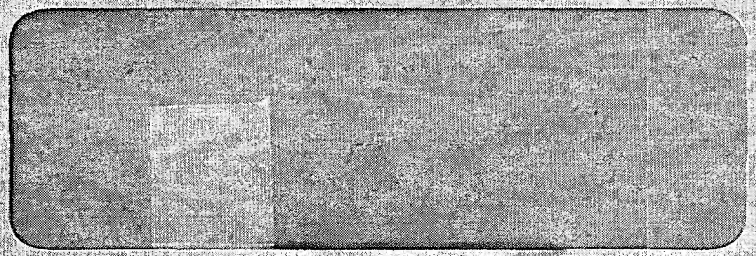

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,402	09/17/2001	Julio Cesar Aguilar Rubido	976-11 PCT/US	3056

7590 03/23/2004

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,402	AGUILAR RUBIDO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-18,21-27 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18, 21-27, 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In the paper submitted December 12, 2003, applicant amended claims 15, 17, 38, 39, 40 and added new claim 42. Claims 15-18, 21-27 and 38-42 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 remains rejected and new claim 42 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 42 is drawn to a method of treating and preventing a viral infection by mucosally administering a vaccine formulation comprising HBsAg and a virus nucleocapsid or a virus-like particle. The nature of the claim is drawn to treating or preventing any viral infection or disease caused by a viral infection. The vaccine art does not teach a vaccine formulation containing viral subunits capable of treating and preventing any viral infection or viral-associated disease. The assertion that the instant formulation is suitable to treat or prevent viral infection necessarily requires evidence to support applicant's assertion. While the working examples discuss the immunoenhancing effects of the instant composition in mice, there is no evidence presented that would indicate that mice developed an immune response sufficient to treat or prevent any viral infection. Since the art does not disclose a single therapeutic or preventive agent that ameliorates

and prevents any viral infection, the skilled artisan would not predict, in the absence of proof to the contrary, that the active agent(s) instantly claimed are efficacious in preventing all viral infections. For these reasons, it is determined that the claimed invention would require an undue quantity of experimentation to make and/or use the invention.

With respect to the rejection of claim 28, applicant argues that the instant specification shows an increase in IgG antibody titers in a murine model. Applicant asserts that the murine model is a valid surrogate challenge model, as evidenced by Murata et al. Applicant also provides a figure in exhibit 2, which indicates a reduction in viral load in the ovaries of mice immunized with antigens alone. Applicant states a willingness to provide a declaration. Applicant submits that the teachings of Murata et al. and the data in exhibit 2 would lead to the conclusion by those skilled in the art that the instant composition is enabled as a vaccine.

Applicant's arguments, a review of the data in exhibit 2 and the teachings of Murata et al. have been fully considered, but are found unpersuasive. Example 5 in the specification discusses an increase in IgG titers in mice upon administration of the instant mixture. However, this data is insufficient for indicating that a protective immune response would be observed in humans exposed to wild-type HCV infection. Moreover, the recombinant vaccinia of Murata et al. is not equivalent to wild-type HCV. HCV is a flavivirus while vaccinia is a poxvirus. Each of the viruses have different modes of transmission, replication, infectivity, host specificity, etiology and pathology. While the data of Murata et al. demonstrates protection against a laboratory engineered vaccinia expressing HCV structural proteins in mice, there is no correlation or nexus that can be made from the protection observed with the recombinant vaccinia challenge virus and wild-type hepatitis C viral infection in humans. The data in exhibit 2 is inconclusive because it

is not clear what the component "Co.120" is. Also, lower recombinant vaccinia titers do not indicate a predicative assessment of HCV titers upon administration with the instant composition. The data and references submitted by applicant do not demonstrate an effective HCV vaccine. Therefore, the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15, 16 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Tabor et al. (US 4,547,368) in light of Bowen et al. (Research in Virology. 1992; 143 (4): 269-78 abstract only) for reasons of record.

Applicant treats this rejection as an obvious-type rejection because there is more than one reference present. Applicant argues that Tabor et al. and Bowen et al. constitute nonanalogous art because Tabor et al. discuss hepatitis and Bowen et al. discuss herpes.

In response, the instant rejection, anticipated by Tabor et al. in light of Bowen et al. is proper under 35 USC § 102. MPEP § 2131.01 specifically states that multiple references in a 102 rejection are proper when extra references are cited to show that a characteristic not disclosed in the reference is inherent. This is the situation in the instant case.

Tabor et al. anticipate a combination vaccine formulation comprising a mixture of 20 μg of HBsAg and 50 μg of hepatitis B nucleocapsid, HBcAg, subunits that are administered subcutaneously. The teachings of Bowen et al. are drawn to immune responses generated by

subunit antigens administered through different routes of administration. To demonstrate similarities or differences between different routes of administration of subunit antigens, Bowen et al. had to have administered subunit antigens through different routes. It is irrelevant whether Bowen et al. use different antigens from Tabor et al. because the conclusions of Bowen et al. are applicable to immune responses generated against antigens administered through different means. Bowen et al. teach that subcutaneous and nasally administered antigens generate equivalent immune responses. Bowen et al. conclude a "common immunological system" for subunits administered mucosally or subcutaneously. Since Tabor et al. anticipate subcutaneous delivery of the instant subunit antigen formulation and Bowen et al. demonstrate that subunit formulations delivered mucosally and subcutaneously generate equivalent immune responses, it is maintained that the subunit vaccine formulation of Tabor et al. also generate equivalent immune responses mucosally.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 25, 27 and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabor et al. in light of Bowen et al. as applied to claims 15, 16 and 21-23 above, and further in view of Rose et al. (US 6,153,201) and Hauser et al. (US 5,972,346) for reasons of record.

Applicant argues that since the instantly presented arguments refute the teachings of Tabor et al. and Bowen et al., the instant rejection is obviated.

As discussed above, the arguments presented do not obviate the rejections of record.

Applicant argues the teachings of Rose et al. and Hauser et al. individually. More specifically, applicant argues that there is no suggestion provided in Rose et al. to combine HBsAg with a second and third antigen. Applicant further argues that Hauser et al. do not teach mucosal administration. Applicant also argues that there is no motivation to combine Rose et al. and Hauser et al. because Hauser et al. do not discuss HPV as one of the other antigens.

Applicant's arguments have been fully considered, but are found unpersuasive. First, if Rose et al. taught all of the instant limitations, the reference would have been applied under 35 USC § 102. As to the mucosal deficiency of Hauser et al., Tabor et al. in light of Bowen et al. teach mucosal administration. Hauser et al. only need teach limitations not previously taught and provide motivation for one skilled in the art to combine the teachings with other references with a reasonable expectation of success. These required elements to establish a prima facie case of obviousness have been established. It is recognized that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the HBsAg and HBcAg antigens of Tabor et al. in light of Bowen et al. with the HPV VLP of Rose et al. to simultaneously treat or prevent hepatitis B and papillomavirus infections. Hauser et al. specifically teach combination vaccines with HBV. Contrary to applicant's assertions, Hauser et al. do not teach away from

combining HPV with HBV. In the excerpt quoted by applicant, Hauser et al. explicitly teach that the hepatitis vaccine formulation is combined with "at least one other component selected from other hepatitis antigens...or non-hepatitis antigens" (emphasis added). Although Hauser et al. do not list HPV, the broad range of other pathogen antigen examples acceptable for combination with the vaccine does not exclude other "non-hepatitis antigens" not specifically listed.

Claims 15, 18 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wands et al. (US 6,025,341) for reasons of record.

Applicant argues that there must be apparent motivation to convert fused antigens to unfused antigens to establish a prima facie case. Applicant further argues that Wands et al. teach away from a protein mixture and cites column 6, lines 45-55.

Applicant's arguments have been fully considered, but are found unpersuasive. In the passage cited by applicant, Wands et al. are discussing a way to get the HCV core protein out of the cell once it is expressed from the recombinant DNA vaccine administered to the host. Applicant has identified yet another step that would be eliminated by directly administering the fusion protein of Wands et al. As stated in the previous rejection, one skilled in the art would be motivated to eliminate the step of using host cell machinery to generate the fusion protein that elicits an immune response. Simultaneous administration of unfused HBsAg and HCV core antigens in a mixture would be equivalent to administering the fusion protein of Wands et al. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Therefore, the invention as a whole would have been prima facie obvious, absent unexpected results to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley

3/22/04

JAMES HOUSEL
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